



LETTER TO THE EDITOR

Challenges in the use of intravenous albumin in critically ill patients: Reflections and future perspectives



Desafíos en el uso de albúmina intravenosa en pacientes críticamente enfermos: reflexiones y perspectivas futuras

Recently, *The International Collaboration for Transfusion Medicine Group* has published the management guides on intravenous albumin.¹ The authors state that in adult critically ill patients, intravenous albumin is not advised as a first option for volume replacement or for elevating the serum albumin levels, independently of the presence of thermal injuries or acute respiratory distress syndrome (ARDS). Likewise, intravenous albumin with diuretics for eliminating extravascular fluid in this population is not advised. These recommendations are based on a moderate to very low certainty of evidence of effect, however.

On one hand, most studies in this field are fundamental upon ambitious medium and long-term effects, such as mortality (mainly at 28 days), the need for renal replacement therapy, or days without mechanical ventilation during admission to the Intensive Care Unit (ICU). However, it must be considered that the administration of high-concentration intravenous albumin causes significant plasma expansion (over 200%), with a peak effect 20 min after infusion and a duration of 5 h.²

On the other hand, the heterogeneity of trans-capillary leakage, which can increase up to 300% in septic shock, may in a different way saturate the absorption capacity of the lymphatic system. It is not possible to establish which patients could benefit most from resuscitation measures with albumin based on inflammatory damage to the endothelial barrier and glycocalyx.³ Albumin use could be appropriate for bleeding resuscitation in cirrhotic patients during liver surgery, or in heart surgery.⁴

The optimum timing of switching from crystalloids to albumin is still the subject of debate. As an example, the SAFE and ALBIOS studies administered albumin within 28 days after patient randomization, while the RASP study did so in the 6 h after randomization. No randomized controlled

trial has evaluated the optimum timing of albumin administration during fluid resuscitation. Regarding the combination of crystalloids and albumin, a recent retrospective analysis of fluid resuscitation in septic patients of the MIMIC-IV database found that individuals receiving the combination in the first 24 h presented a significantly lower mortality rate at 28 days (12.5% versus 16.4%; $p = 0.003$).^{5,6}

It also must be mentioned that the administration of chloride-rich fluids has been related to adverse events in the critically ill. Some commercial solutions of low-concentration albumin (4–5%) contain high chloride concentrations. In comparison, 20% albumin with limited chloride levels has been associated with a significantly lesser incidence of hyperchloremia.⁷

It is clear that the cost of albumin may be 40–80 times higher than that of a crystalloid. In a cost-benefit analysis based on the *post hoc* analysis of the ALBIOS study in septic patients, the additional cost per life saved was 14,384 dollars in 2017.⁸

In view of the above, we consider it necessary to carry out studies centered on proportional effects to evaluate the role and timing of albumin administration as rescue fluid in septic patients that do not respond to initial resuscitation measures with crystalloids,⁹ particularly considering the considerably higher cost of albumin compared with crystalloids.

Funding

The present article has received no financial support.

Author contribution

All the signing authors meet the **requirements of authorship**. The study complies with the Good Clinical Practice guidelines.

Alejandro González-Castro: Conception, development and writing of the manuscript.

Raquel Ferrero-Franco: Conception and correction of the manuscript.

Carmen Blanco-Huelga: Conception. Preparation of the bibliography.

Conflicts of interest

All authors declare that they have no conflict of interest.

DOI of original article: <https://doi.org/10.1016/j.medin.2024.03.016>

<https://doi.org/10.1016/j.medicine.2024.04.016>

2173-5727/© 2024 Elsevier España, S.L.U. and SEMICYUC. All rights reserved.

References

1. Callum J, Skubas NJ, Bathla A, Keshavarz H, Clark EG, Rochwerg B, et al. ICTMG Intravenous Albumin Guideline Group. Use of intravenous albumin: a guideline from the International Collaboration for Transfusion Medicine Guidelines. *Chest*. 2024;4, <http://dx.doi.org/10.1016/j.chest.2024.02.049>. S0012-3692(24)00285-X.
2. Zdolsek M, Hahn RG, Zdolsek JH. Recruitment of extravascular fluid by hyperoncotic albumin. *Acta Anaesthesiol Scand*. 2018;62:1255–60, <http://dx.doi.org/10.1111/aas.13150>.
3. Joannidis M, Wiedermann CJ, Ostermann M. Ten myths about albumin. *Intensive Care Med*. 2022;48:602–5, <http://dx.doi.org/10.1007/s00134-022-06655-8>.
4. Llau JV, Aldecoa C, Guasch E, Marco P, Marcos-Neira P, Paniagua P, et al. Multidisciplinary consensus document on the management of massive haemorrhage. First update 2023 (document HEMOMAS-II). *Med Intensiva (Engl Ed)*. 2023;47:454–67, <http://dx.doi.org/10.1016/j.medine.2023.03.019>.
5. Sa MB, Salaverría I, Cabas AC. Fluidoterapia en la sepsis y el shock séptico [Fluid therapy in sepsis and septic shock]. *Med Intensiva (Engl Ed)*. 2022;46:14–25, <http://dx.doi.org/10.1016/j.medine.2022.03.009>.
6. Zhou S, Zeng Z, Wei H, Sha T, An S. Early combination of albumin with crystalloids administration might be beneficial for the survival of septic patients: a retrospective analysis from MIMIC-IV database. *Ann Intensive Care*. 2021;11:42, <http://dx.doi.org/10.1186/s13613-021-00830-8>.
7. SAFE Study Investigators, Australian and New Zealand Intensive Care Society Clinical Trials Group, Australian Red Cross Blood Service, George Institute for International Health, Myburgh J, Cooper DJ, Finfer S, Bellomo R, Norton R, Bishop N, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med*. 2007;357:874–84, <http://dx.doi.org/10.1056/NEJMoa067514>.
8. Joint Formulary Committee. *British national formulary*. 79th ed. London: BMJ Group and Pharmaceutical Press; 2020.
9. Del Río-Carbajo L, Nieto-Del Olmo J, Fernández-Ugidos P, Vidal-Cortés P. Resuscitation strategy for patients with sepsis and septic shock. *Med Intensiva (Engl Ed)*. 2022;46:60–71, <http://dx.doi.org/10.1016/j.medine.2022.02.025>.

Alejandro González-Castro^{a,*}, Raquel Ferrero-Franco^b, Carmen Blanco Huelga^a

^a *Servicio de Medicina Intensiva, Hospital Universitario Marqués de Valdecilla, Santander, Spain*

^b *Servicio Cántabro de Salud, Santander, Spain*

* Corresponding author.

E-mail address: e409@humv.es (A. González-Castro).